

Appendix (Appendix Supplementary Tables and Figures)

Appendix Supplementary Table 1: PEGASUS Program Development and Implementation Milestones

1. Organizational readiness	<ul style="list-style-type: none"> • Approvals from hospital leadership and relevant councils • Physician and nurse clinician champions from emergency department, anesthesiology, critical care, neurosurgery, general surgery • Recurrent interdisciplinary stakeholder meetings • Departmental agreements
2. Climate survey	<ul style="list-style-type: none"> • Test TBI guideline knowledge, attitudes and beliefs; share results • Elicit provider identified gaps in TBI care • Survey of clinicians and allied health providers
3. TBI guideline education	<ul style="list-style-type: none"> • Discuss strength of evidence, and willingness to adopt protective KPIs • Physician consensus on KPIs
4. Identification of multilevel barriers	<ul style="list-style-type: none"> • Facilitated focus groups • Develop domains for barriers and facilitators • Develop strategies to redress barriers and promote TBI guideline adherence • Quality improvement process PDCA cycle
5. Promotional material and pathway formats	<ul style="list-style-type: none"> • Promotional materials, location, format • Format for clinical care pathway
6. Validation of retrospective study findings	<ul style="list-style-type: none"> • Prospective validation of KPIs in 14 patients
7. Program implementation	<ul style="list-style-type: none"> • Includes <ul style="list-style-type: none"> ○ Pathway (the what) ○ Process (the how) ○ Perspectives (the common goal)
8. Clinical care pathway	<ul style="list-style-type: none"> • Value stream mapping • Consideration of task order • ED, OR, PICU and ward <ul style="list-style-type: none"> ○ Paper pathways (ED, PICU, ward) ○ Activated decision support for OR • Flexible start and stop based on severe TBI diagnosis • Initiated by PICU nurse • Paper packet with one sheet per PICU day • Duration of PICU LOS • Daily checkboxes with goals • Nursing documentation of task completion and efforts made

	<ul style="list-style-type: none"> • Physician documentation of pathway on admission and on daily rounds. • Free text space to write in comments • Email feedback to PEGASUS administrative team after pathway use • Communication steps and scripts • Timelines for family conferences • Pager numbers for clinicians • PEGASUS sign on patient door
9. Implementation fidelity measures	<ul style="list-style-type: none"> • Organizational: Reports, meetings • Physician: attending or resident documentation of “PEGASUS pathway” participation in electronic record. • Nursing: <ul style="list-style-type: none"> ○ ED pathway completion ○ Pathway start in first 24 hours of admission ○ PICU nurse completion of pathway tasks or explanations for not doing so ○ Use of pathway through PICU discharge ○ Return of pathway at PICU discharge
10. Data sharing and rewards	<ul style="list-style-type: none"> • Annual departmental conference presentations, nursing staff meetings • Quarterly trauma council and pediatric committee report • Internal quality improvement dashboard for KPI guideline adherence • Posters and recognition events
11. Feasibility and sustainability	<ul style="list-style-type: none"> • Bi-monthly census checks • Bi-monthly pathway checks • 3-month Plan Do Check Act cycles
12. Provider satisfaction	<ul style="list-style-type: none"> • Attending, and resident satisfaction surveys for refinement for each of first 20 patients, then quarterly for one year • Documentation of changes in between and within team communications

Appendix Supplementary Table 2: A Priori List of Potentially Outcome-associated Covariates and Selection Processes by Best Subsets Leaps-and-bounds Algorithm for Each Adjusted Model.

A priori selected covariate	Model a (dose-response)		Model b (KPI-hypocarbia)		Model c (KPI-CPP)		Model d (KPI-nutrition)		Model e (3 KPIs)	
	S*	D**	S*	D**	S*	D**	S*	D**	S*	D**
Age			+	+				+	+	
Sex										
Abusive TBI	+	+	+	+	+	+	+	+		+
Poly trauma					+		+			
AIS-head	+	+	+	+	+	+	+	+	+	+
AIS-abdomen			NA	NA	NA	NA				
Highest non-head AIS		+	+	+	+	+	+	+		+
ED Total GCS	+	+	+	+	+	+	+	+	+	
Adjusted R ²	0.32	0.46	0.11	0.37	0.24	0.32	0.42	0.35	0.55	0.50

Abbreviation: AIS, abbreviated injury score

* Hospital discharge survival as the dependent variable in corresponding models.

** Favorable hospital discharge disposition as the dependent variable in corresponding models.

Appendix Supplementary Table 3: Patients Pre-and Post-PEGASUS Program Participation

	Pre-Program Patients 12/2006 - 04/2011 n=56^a	Program participants Strict inclusion criteria^b 5/2011 - 07/2017 n=71^b	Program participants Extended inclusion criteria 5/2011 - 07/2017 n=199^c
Inclusion criteria	Admission GCS ≤ 8 , AIS ≥ 3 , mechanical ventilation ≥ 48 hours, survived ≥ 72 hours		Any GCS ≤ 8 and TBI diagnosis
Age (yr), median (IQR)	14·8 (11·2)	14·8 (11·2)	11·9 (12·7)
Male Sex, n (%)	41 (73·2)	50 (70·4)	141 (70·9)
Injury Mechanism, n (%)			
<i>Motor vehicle crash</i>	24 (42·9)	26 (36·6)	66 (33·2)
<i>Fall</i>	10 (17·9)	18 (25·4)	49 (24·6)
<i>Struck by vehicle</i>	10 (17·9)	17 (23·9)	41 (20·6)
<i>Abusive TBI</i>	4 (7·1)	3 (4·2)	15 (7·5)
<i>Sport/Recreation</i>	2 (3·6)	2 (2·8)	15 (7·5)
<i>Gunshot</i>	3 (5·4)	4 (5·6)	12 (6·0)
<i>Other</i>	3 (5·4)	1 (1·4)	1 (0·5)
EMS GCS, median (IQR)	5 (4·0)	3 (4·5)	3 (4·5)
Pediatric Trauma Score, Median (IQR)	2 (4·0)	3 (3·0)	3 (3·0)
Transport Type, n (%)			
<i>Ambulance</i>	22 (39·3)	24 (34·3)	81 (41·1)
<i>Helicopter</i>	21 (37·5)	18 (25·7)	58 (29·5)
<i>Fixed Wing Aircraft</i>	13 (23·2)	27 (38·6)	57 (28·9)
<i>Personal Vehicle</i>	0 (0)	1 (1·4)	1 (0·5)
Advanced Life Support Transport n (%)	56 (100)	65 (92·9)	181 (91·9)
Intubated on Admit[#], n (%)	Not Available	68 (95·8)	186 (93·5)
ED admit Glasgow Coma Scale score, median (IQR)	6 (4)	4·5 (4)	6 (4)
ED Glasgow Coma Scale (admit motor), median (IQR)	1 (0)	1 (0)	1 (0)
PICU Glasgow Coma Scale, median (IQR) (admit total), n (%)	6 (5)	6 (3)	8 (5·0)
Discharge Glasgow Coma Scale (motor), median (IQR)	5 (1)	6 (1)	6 (0)
Head Abbreviated Injury Scale (AIS), Median (IQR)	5 (1)	5 (1)	5 (1·0)
Non-head highest AIS, median (IQR)	3 (2·3)	3 (2·0)	2 (2·0)
Injury severity score (ISS),	36·5 (18)	33 (16)	29 (16·0)

median (IQR)			
Admitted to the OR prior to PICU	19 (33·9%)	27 (38·0%)	61 (30·7%)
Polytrauma, n (%)	40 (71·4)	38 (53·5)	86 (43·2)
Any surgery, n (%)	42 (75·0)	36 (50·7)	122 (61·3)
Craniotomy, n (%)	11 (19·6)	29 (40·8)	56 (28·1)
Intracranial Pressure Monitoring, n (%)	48 (85·7)	52 (70·8)	72 (36·1)
No brain herniation, n (%)	37 (66·1)	35 (49·3)	105 (52·8)
Avoided unwanted Hypocarb^a, n (%)	18 (64·3)	21 (60·0)	76 (72·4)
Maintained all CPP, n (%)	36 (64·3)	42 (60·0)	127 (64·3)
Early nutrition Start, n(%)	52 (92·9)	69 (97·2)	162 (81·4)
Hospital discharge survival, n (%)	51 (91·15)	64 (90·1)	160 (80·4)
Favorable hospital discharge disposition, n (%)	31 (55·4)	45 (63·4)	135 (67·8)

Abbreviation SD, standard deviation; IQR, interquartile range.

High degree of missingness in data (>20% missing). Data not available for Pre-Program patients.

^a Local subset of patients previously reported. ³

^b Subset of program participants who met strict inclusion criteria

^c Program participants with liberalized use criteria and completed clinical care pathways

Appendix Supplementary Table 4. Traumatic Brain Injury (TBI) Severity of 199 PEGASUS Program Participants at Admission to Emergency Department (ED), Pediatric Intensive Care Unit (PICU), and at Discharge. TBI severity is defined by total Glasgow Coma Scale score closest to each of these timed events, irrespective of change in category between these time points. The GCS score is not static and patients can enter and exit the severe TBI category. The pathway, then, can be initiated and terminated when bedside clinicians consider patients eligible after hospital admission and prior to hospital discharge. The number of patients who had $GCS \leq 8$ and received severe TBI care at some point in hospital (n=193) exceeds those with a recorded discharge diagnosis of severe TBI.

	<i>Mild^a</i>	<i>Moderate^b</i>	<i>Severe^c</i>
<i>ED Admit (N = 199)</i>	5 (2·51%)	19 (9·55%)	175 (87·94%)
<i>PICU Admit (N = 199)</i>	22 (11·06%)	63 (31·66%)	114 (57·27%)
<i>Hospital Discharge (N = 199)*</i>	114 (57·27 %)	24 (12·06 %)	61 (30·65%)

*31 (15·6%) patients died

^a Glasgow Coma Score 14 – 15

^b Glasgow Coma Score 9 – 13

^c Glasgow Coma Score ≤ 8

Appendix Supplementary Table 5. Dose-Response to Key Performance Indicator (KPI) Adherence and Discharge Outcomes. N = 105 program participants without brain herniation.

Adherence to Number of KPIs	<i>Survival</i> N (%)	Unadjusted RR [95% CI]	Adjusted RR* [95% CI]	<i>Favorable disposition</i> N (%)	Unadjusted RR [95% CI]	Adjusted RR** [95% CI]
0 (n=4)	0 (0)			0 (0)		
1 (n=13)	10 (76·9)	1·27	1·25	5 (38·5)	1·46	1·29
2 (n=44)	40 (90·9)	[1·12-1·44]	[1·10-1·42]	36 (81·8)	[1·23-1·72]	[1·10-1·51]
3 (n=44)	44 (100)			40 (90·9)		

Abbreviation: RR, Risk ratio.

All RR estimated by modified Poisson regression; survival and favorable disposition were dichotomous, while number of achieved KPI was coded as a continuous variable. Dose-responsive patterns were also demonstrated when KPI was coded as dummy variables.

Sub-analysis on all patients before and after program implementation demonstrated similar results.

*Adjusted for abusive TBI, head AIS and ED GCS selected by best subsets leaps-and-bounds algorithm.

** Adjusted for abusive TBI, head AIS, highest non-head AIS and ED GCS selected by best subsets leaps-and-bounds algorithm.

Appendix Supplementary Table 6. Discharge Outcome of PEGASUS Program Participants by Combination of Key Performance Indicators (KPIs). N =105 program participants without brain herniation.

KPI Adherence			Discharge Outcome		
Early nutrition Start ^a	Maintain all CPP ^b	Avoid any unwanted hypocarbia ^c	Patients (N)	Survival N (%)	Favorable disposition N (%)
Yes	Yes	Yes	44	44 (100)	40 (90·9)
Yes	Yes	No	17	17 (100)	15 (88·2)
Yes	No	Yes	22	20 (90·9)	18 (81·8)
No	Yes	Yes	5	3 (60)	3 (60)
Yes	No	No	7	7 (100)	4 (57·1)
No	Yes	No	1	0 (0)	0 (0)
No	No	Yes	5	3 (60)	1 (20)
No	No	No	4	0 (0)	0 (0)

^a Start of either enteral or parenteral nutrition within first 72 hours after severe TBI diagnosis.

^b Maintenance of all CPP > 40mmHg during first 72 hours after severe TBI diagnosis.

^c Avoidance of any unwanted PaCO₂ < 30mmhg in the absence of brain herniation; only includes patients without herniation.

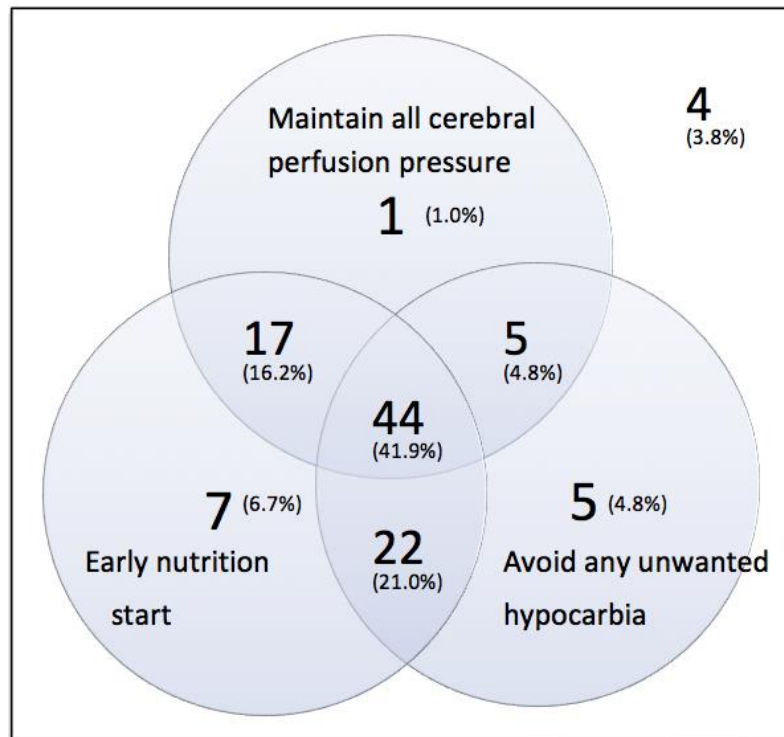
Supplemental Table 7. Discharge Outcomes in Participants Achieving and Not Achieving Adherence to Key Performance Indicators for Cerebral Perfusion Pressure (KPI-CPP) by Intracranial Pressure (ICP) Monitor Placement Status. Chi square test $p = 0.42$ for survival and $p = 0.05$ for disposition.

	Adherence to KPI-CPP*	Non-adherence to KPI-CPP
ICP monitoring (N=72)	40/42 (95.2%)	24/30 (80.0%)
	Discharge survival	Discharge survival
No ICP monitoring (N=127)	73/86 (84.9%)	23/41 (56.1%)
	Discharge survival	Discharge survival
ICP monitoring (N=72)	31/42 (73.8%)	19/30 (63.3%)
	Favorable discharge disposition**	Favorable discharge disposition
No ICP monitoring (N=127)	68/86 (79.1%)	17/41 (41.5%)
	Favorable discharge disposition	Favorable discharge disposition

* Maintenance of all CPP > 40mmHg during first 72 hours after severe TBI.

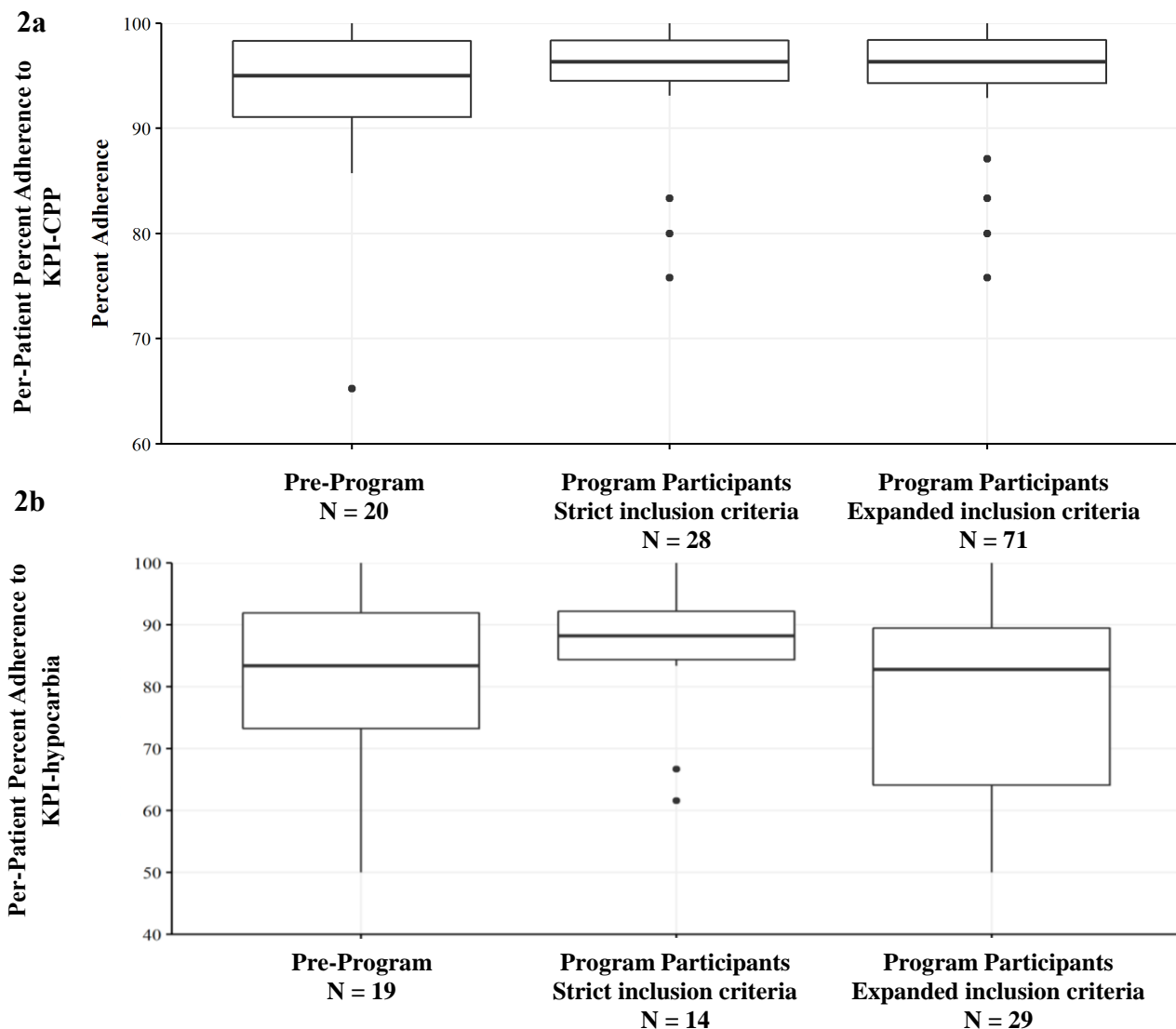
** Defined as discharged home and inpatient/outpatient rehabilitation.

Supplemental Figure 1: Achieving Adherence to Key Performance Indicators (KPI) during the first 72 hours after Severe Traumatic Brain Injury Diagnosis among PEGASUS Program Participants. N = 105 program participants without brain herniation. Maintain all cerebral perfusion pressure defined as maintenance of all CPP > 40mmHg for 72 hour from severe TBI diagnosis. Early nutrition start defined as initiation of enteral or parenteral nutrition within 72 hours of severe TBI diagnosis. Avoid any unwanted hypocarbia defined as maintenance of all PaCO₂ > 30mmHg in absence of cerebral herniation for 72 hours from severe TBI diagnosis.



Supplemental Figures 2a and 2b: Distribution of (2a) Cerebral Perfusion Pressure and (2b) PaCO₂ Values Among Participants Who Did Not Achieve 100% Key Performance Indicator Adherence during the First 72 hours after Severe Traumatic Brain Injury Diagnosis.

A) Patients are a subset; those who did not achieve 100% adherence to KPI-CPP (KPI adherence for CPP defined as maintenance of all cerebral perfusion pressure (CPP > 40mmHg)). Pre-program N = 20/56, program participants meeting strict criteria 28/71, program participants expanded criteria N=71/199. One pre-program patient and one patient in the program had no adherent KPI values, despite multiple data points. Both patients with zero percent adherence died. Quantile regression revealed no significant difference in lower side of the IQR (25th percentile) between pre-program (90·4%) and program participants meeting strict inclusion criteria (94·2%) (p = 0·78). **B)** Patients are a subset; of those who did not achieve 100% adherence to KPI-hypocarbica of the N = 37, 35, and 105 patients without brain herniation; KPI adherence for PaCO₂ defined as avoidance of any hypocarbica (PaCO₂ < 30mmHg) in those without brain herniation. Six patients in the Program had no adherent PaCO₂ values but had only one value drawn throughout hospital stay. Quantile regression revealed no significant difference in lower side of the IQR (25th percentile) between pre-program (71·4%) and program participants meeting strict inclusion criteria (83·3%) (p = 0·64).



Supplemental Figures 3a and 3b. Relative Contribution of Each Key Performance Indicator (KPI) to (3a) Survival and (3b) Discharge Disposition. N =105 program participants without brain herniation. All three KPIs included in a single model and coded as dummy variables. Favorable discharge disposition defined as discharge to home or inpatient/outpatient rehabilitation. Avoid any unwanted hypocarbia defined as maintenance of all PaCO₂ > 30mmHg for 72 hours from severe TBI diagnosis in absence of cerebral herniation. Maintain all cerebral perfusion pressure defined as maintenance of all CPP > 40mmHg for 72 hour from severe TBI diagnosis. Early nutrition start refers to the initiation of enteral or parenteral nutrition within 72 hours of severe TBI diagnosis. (covariate selected by best subsets leaps-and-bounds algorithm for adjusted model: survival-age, head AIS and ED GCS; disposition-abusive TBI, head AIS and highest non-head AIS). Abbreviation: RR, Risk ratio; CPP, cerebral perfusion pressure; AIS, Abbreviated Injury Score.

